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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,356	05/09/2001	Martin A. Cheever	014058-009811US	1297

23347 7590 08/31/2007

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	
MAIL DATE	**DELIVERY MODE**
08/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/854,356	CHEEVER ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/28/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *113,116-125 and 146-156* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *113,116-125 and 146-156* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/13/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/29/07 has been entered.

2. Claims 114 and 145 were cancelled and Claims 113, 116, 117 and 146 are amended in the Response of 6/29/07.

3. Claims 113, 116-125 and 146-156 are all the pending claims for this application and all the claims under examination.

Withdrawal of Rejections

35 USC § 112-second paragraph

4. The rejection of Claims 113, 114, 116-125 and 145-156 under 35 U.S.C. 112, second paragraph, for the recitation "a protein comprising a contiguous amino acid sequence" is withdrawn and moot in view of cancelled Claims 114 and 145, and withdrawn for Claims 113, 116-125 and 146-156 in view of the deletion of the phrase from Claims 113 and 116. Applicants' comments on pp. 6-7 of the Response of 6/28/07 have been considered and entered.

35 USC § 112-first paragraph

Written Description

5. The rejection of Claims 114 and 145 under 35 U.S.C. 112, first paragraph, as lacking written description support for "a protein comprising a contiguous amino acid sequence having SEQ ID NO: 6" or "SEQ ID NO:7" is withdrawn and moot in view of the cancelled claims.

Enablement

6. The rejection of Claims 114 and 145 under 35 U.S.C. 112, first paragraph, in lacking enablement for using the composition in a vaccine for inducing a specific prophylactic immune response for any disease or disorder in a warm-blooded animal is withdrawn and moot in view of the cancelled claims. Applicants' comments on p. 9 of the Response of 6/28/07 have been considered and entered.

Rejections Maintained

35 USC § 112-first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

7. The rejection of Claims 113, 116-125 and 146-156 under 35 U.S.C. 112, first paragraph, in lacking written description support for "a protein comprising a contiguous

amino acid sequence having SEQ ID NO: 6" or "SEQ ID NO: 7" is withdrawn in part for the deletion of the phrase "contiguous" but maintained because the instant generic claims, 113 and 116, recite "comprising" language that reads on any polypeptide having within its amino acid sequence a region consisting of either SEQ ID NO:6 or 7.

Claims 113 and 116 now recite that "a polypeptide comprising the amino acid sequence of SEQ ID NO: 6, where SEQ ID NO:6 (or 7) is administered." For reasons of record and as restated hereinafter, the claims are drawn to a genus of polypeptides that was not described or envisioned at the time of application filing.

The specification teaches a total of three HER2 proteins: 1) the full length Her-2/neu protein (SEQ ID NO:1), 2) the Her-2/neu fusion protein comprising SEQ ID NO: 6 (919 amino acid residues; the extracellular domain (ECD) and the phosphorylation domain (PD), and 3) the Her-2/neu fusion protein of SEQ ID NO:7 (712 amino acid residues; the extracellular domain (ECD) and a preferred portion of the phosphorylation domain(ΔPD) of the human HER-2/neu protein (SEQ ID NO:7). The specification does not disclose or contemplate any other proteins containing amino acid residues of SEQ ID NO: 6 or 7.

Applicants' allegations on pp. 7-9 have been considered but are not found persuasive. Applicants state "the structure of SEQ ID NO: 6 or 7 elicits or enhances the immune response to HER2/neu" (bottom p. 7), "the exact sequence of both SEQ ID NO: 6 and 7 is provided; the function of eliciting an immune response to HER2/Nue is also described" (center of p. 8), and "in the present claims, the functional characteristic (inducing an immune response) is directly related to the recited structure (SEQ ID NO:6

or 7)" (p. 9). Applicants statement of record supports the Examiner's position that the polypeptide consisting of SEQ ID NO: 6 or 7 would meet the requirements under 35 U.S.C. 112, namely, having a structure and function defined by the original specification. For these reasons, the rejection is maintained.

Enablement

8. The rejection of Claims 113, 155, 116 and 156 under 35 U.S.C. 112, first paragraph, in lacking enablement for using the method to elicit or enhance an immune response in a human is maintained.

Applicants' allegations on pp. 10-13 of the Response of 6/28/07, the Limentani Abstract and the 1.132 Declaration of Dr. Jamila Louahed have been considered but are not persuasive.

In brief, the Kurebayashi reference (Exp. Opin. Pharmacother. 1(4):603-614 (2000); cited in the IDS of 6/13/07) is discussed on pp. 11-12 of the Response and is alleged to describe the state of art in immunotherapeutics for HER2-expressing breast cancer with respect to the recognition of naturally occurring HER2 antibodies in breast cancer patients. Kurebayashi predicts that vaccines will promote immunity to HER2 but specifically states that it is unknown whether immunity to HER2 predicts improved survival. Taken alone, Kurebayashi is not persuasive evidence that an attenuated form of HER2 as recited in the instant claims could generate or enhance an immune response in a human, and what an effective amount would be for achieving this endpoint.

The abstract of Limentani (J. Clin. Oncol. 24(18S): 631 (2006); cited in the IDS of 6/13/07) and a reference to a corresponding Poster (no copy of which is provided) is discussed on p. 12 of the Response and is alleged to describe treating Stage II and Stage III Her2+ breast cancer in human patients with the 919 amino acid sequence of SEQ ID NO:6 in combination with adjuvant AS15. The abstract states that the "*ECD/ICD*" polypeptide/adjuvant elicits an immune response recorded as an anti-ECD antibody that bound the HER2 receptor and a specific T cell response, and where two metastatic patients showed tumor regression. However, it is noted that an "*ECD/ICD*" polypeptide would not correspond to an ECD/PD polypeptide of SEQ ID NO:6. On p. 7 of the specification, an "ECD/ICD" fusion protein is specifically defined as "comprising the extracellular domain and the intracellular domain of the HER2/neu protein" and that an "ECD/ICD protein does not include a substantial portion if any of the HER2/neu transmembrane domain." Then in the next paragraph, the "ECD/PD" or ECD/ΔPD" is specifically defined as "comprising the extracellular domain and phosphorylation domain" and that an "ECD/PD and ECD/ΔPD protein does not include a substantial portion if any of the HER2/neu transmembrane domain." In the center of p. 8 of the Response of 6/28/07, Applicants specifically refer to fusion proteins combining ECD with PD as the preferred form. Based on these definitions of record and absent further evidence to the contrary, it is not understood how the "ECD/ICD" protein of the Limentani abstract could be the same as the 919 amino acid sequence of SEQ ID NO:6.

In the 1.132 Declaration, Dr. Louahed avers that he/she is employed by the assignee for the instant application, and states that the therapeutic composition

comprising ECD/ICD provided to the human HER2+ breast cancer patients described in the Limentani Abstract for the related poster is the same polypeptide of SEQ ID NO:6 as described in the specification. As stated supra, it is noted that throughout the specification an ECD/PD polypeptide is defined by SEQ ID NO: 6, therefore, it is unclear what polypeptide is encompassed by the Limentani abstract and the Louahed declaration.

The conclusion that the newly submitted evidence appears to contradict the disclosure in the specification is based on the totality of the evidence. Thus the rejection that attenuated forms of HER2, namely, a polypeptide of SEQ ID NO: 6 or 7, could have an immune eliciting or enhancing effect in a human patient is maintained (In re Piasecki, 223 USPQ 785 (Fed. Cir. 1984); In re Semaker, 217 USPQ 1 (Fed. Cir. 1983).

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 113, 116-125 and 146-156 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 113 and 117-125 are indefinite for the recitation "where said SEQ ID NO: 6 is administered" in Claim 113, and Claims 116 and 146-156 are indefinite for the recitation "where said SEQ ID NO: 7 is administered" in Claim 116 because it is unclear

if SEQ ID NO: 6 or 7 is administered or a polypeptide comprising SEQ ID NO: 6 or 7. Rewriting the claims to recite that the respective composition or the polypeptide comprising the composition is administered in an immune response eliciting or enhancing amount could overcome the rejection.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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